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Scaffold-Optimized Dendrimers for the Detection of the Triacetone Triperoxide Explosive Using Quartz Crystal Microbalances

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Triacetone triperoxide (TATP; Scheme 1) is an explosive made from common household chemicals. The sensitivity towards shock, friction, and electrostatic ignition makes this explosive



 $\mbox{Scheme 1. Structure of triacetone triperoxide (TATP) and the reference dendrimer <math display="inline">1.^{\mbox{\tiny TATP}}$

extremely dangerous.^[1] TATP and related compounds have experienced significant attention as a threat in terrorist attacks.^[2] It is considered as the prime material among home-made explosives.^[1,3] Compared to other explosives TATP exhibits an unusually high vapor pressure of approximately 68-78 ppm under ambient conditions.^[4] Therefore, the direct tracing of airborne material should be possible. The majority of analytical methods for the detection of TATP relies on the analysis of H₂O₂ after hydrolysis or dissociation of the explosive.^[5a-f] For such a detection of TATP, two major drawbacks occur: First, initial removal of H₂O₂ which is ubiquitous in our daily life; second, longtime sampling of analyte in order to have sufficient material for the detection process. These approaches are time-consuming and not feasible for a low-cost sensor technology. Only few methods directly detect TATP.^[5g-i] Recently, our research group has demonstrated that quartz crystal microbalances (QCM) are a suitable low-cost technology platform for a continuously working sensor to trace TATP.^[6] High fundamental

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frequency QCM (ca. 200 MHz) can be coated with affinity materials and enable the detection of airborne sources on a picogram scale within seconds.^[7] If a suitable coating is chosen, then high sensitivity and selectivity is given. The affinity material deposited on the electrode surface of the QCM creates a signal based on the desired chemisorption upon binding of the analyte.^[8a-c] In general, this interaction is interfered with an unselective physisorption,^[8b] which is often dominated by humidity. However, the key for a powerful sensor based on QCM requires coating exhibiting a high affinity and selectivity for the desired analyte.^[9] The enhanced quality of such coatings facilitates subsequent application in sensor arrays involving several QCM.

Consequently, the affinity material plays an utmost and crucial role which is the key within this interdisciplinary sensor project. The supramolecular interaction of the analyte with the affinity material exploits the reversible nature of noncovalent binding and provides a fast recovery of the sensor in an air stream.

In previous studies, we identified a variety of suitable affinity materials for TATP with a complementary cross-affinity to interfering compounds.^[6] Among these coatings, polyphenylene dendrimers turned out to exhibit the strongest binding capability for TATP while the signals for H₂O and H₂O₂ are very low. The best properties were found with **1** (Scheme 1). The outstanding affinity was attributed to the complementary voids in the dendrimer and binding through CH– π - and dipole–dipole interactions on the pyridine moieties at the interior of the dendritic core–shell architecture.

Herein, we present a significant improvement in affinity and selectivity by molecular variation of the new dendritic polyphenylene-structures by equipping the inner shells with diverse substituents (pyrenyl, pyridyl, nitro, cyano, and amide moieties). Dendrimers represent a unique class of macromolecules because they offer a branched architecture with multiple end groups and a defined molecular structure.^[11] In the past decades a broad variety of repetitive reaction sequences have been employed for the construction of such systems.^[12] In contrast to other dendrimers containing conformationally very flexible single bonds, the rigidity of the dendritic polyphenylene scaffold limits the conformational freedom because only confined rotation around the biaryl axis can occur.^[13] Owing to their unique shape persistence and monodispersity, polyphenylene dendrimers proved to be perfect candidates for hostguest chemistry.^[14]

For the studies a collection of new polyphenylene dendrimers was synthesized containing a variety of different substituents at the internal branches of the dendrimer architecture. The incorporated moieties are mostly polar and electron withdrawing. The synthetic pathway to these TATP attractive den-

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drimers exploits a reliable and established strategy.^[15] Particular attention has to be given to the cyclopentadienone starting materials **S2–S6** (Scheme 2) which provide upon cycloaddition and subsequent extrusion of carbon monoxide branching into the dendrimer scaffold. The tetraarylcyclopentadienones **S2–S6** were prepared starting from the corresponding 1,2-diketones in a Knoevenagel condensation.^[16] The molecular variation of this building block is focused onto the positions 2 and 5 of the cyclopentadienone (marked as R in Scheme 2), whereas the remaining aryl moieties are equipped with alkyne moieties. After removal of the silyl groups, an iterative installation of subsequent molecular shells was performed. It was demonstrated that tetrahedral polyphenylene dendrimers based on a tetra-



Scheme 2. Synthetic pathway towards substituted polyphenylene dendrimers.

phenylmethane core form cavities,^[17] which display promising shape persistent voids for the uptake of different guests. This fundamental design was maintained throughout our studies. After successful synthesis of the branching units **S2–S6**, iterative assembly of specific dendritic scaffolds was accomplished by a repetitive Diels–Alder approach and subsequent desilylation sequences. Thus dendritic macromolecules could be prepared divergently to the third generation. As depicted in Scheme 2, the sixteen terminal alkynes in the periphery of **11**, were then capped by reaction with tetraphenylcyclopentadienone. The amide dendrimers **7** were obtained by amidation of the corresponding esters **6**. This gives access to **2b–7b**, which exhibit a nonpolar outer shell. The novel G₂ dendrimers **4a**

> contain a doubled number of incorporated pyridine entities per generation compared to **1**. This aspect was of particular interest because the performance of previous affinity materials for quartz micro balances was attributed to this specific moiety. With an increased content an ameliorated inclusion behavior towards TATP was anticipated.

For evaluation of the affinity capabilities of each dendrimer, quartz crystal microbalances with a fundamental frequency of 195 MHz were coated with 2-7. The coating was done by an electrospray protocol.^[18] This particular method guarantees a highly reliable and reproducible deposition of material in the nanogram range. For determination of the affinities to a respective analyte, concentration profiles were measured at 35°C. Therefore, a nitrogen flow was enriched with a defined partial pressure of analyte gas and passed on the coated QCM. From concentration profiles the adsorption isotherms can be obtained.^[17a] The slope of such an isotherm is directly proportional to the affinity of the analyte to the coating material.[19] All dendrimers, except 2a, 6a, and 4b, could be applied as coating material for the QCM. The dendrimers 2a, 6a, and 4b displayed viscoelastic effects during the coating procedure. Consequently, it was not possible to obtain a homogeneous coating using these compounds. Furthermore, the

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standard of the previous studies 1 (Scheme 1) and polyphenylene analogue (12, structure in the Supporting Information) were investigated. With 12 the effect of the functionalizations of the inner shells was explored. The affinities of the dendrimer coatings for TATP are displayed in Figure 1. Dendrimers 4a, 5, 2b, 3b, and 7b show a significantly higher affinity for TATP



Figure 1. Slopes of adsorption isotherms for TATP. Best known system polyphenylen-pyridyl dendrimer 1 is indicated by the horizontal line.

than reference material 1. The effect of different dendrimer generations can be observed for two sets of affinity materials (3 a vs. 3b and 7 a vs. 7b, respectively). These pairs reveal that the G₃ dendrimers, with the larger scaffolds and more pronounced voids, provide the higher affinity. Interestingly, the pyrene-functionalized G₂ compound 5 ranges among the best affinity materials despite the expanded aromatic substituents inside the dendrimer. Owing to the spatial demand of the pyrenyl moieties the large voids in the dendritic scaffold should be more structured. The polycyclic aromatic groups represent electron-rich walls, which provide better niches for accommodating the nonpolar analytes by CH- π contacts (see figures obtained by computational chemistry in the Supporting Information). Consequently, the relatively small G₂ compound 5 is capable of accumulating TATP with an outstanding efficiency. An enhanced affinity for TATP by a factor of two seems at a first sight not significant but improvement of such a highly potent system facilitates the later sensor applications tremendously.

Additional aspects that influence the dendrimer affinities towards analytes are: 1) their electronic properties and thus CH– π interactions between the dendrimer and incorporated guest, and 2) the possibility of hydrogen bonds. The electron-deficient nature of the inner shells has an obvious positive effect on the affinity. Therefore, nitro-, cyano-, and amide-modified G₃ systems (**2b**, **3b**, and **7b**) reveal higher affinities than the unmodified dendrimer **12**. In addition, less electron-rich species show dramatically enhanced long term stability because the QCM are operated at ambient conditions. The coating will consist of a few molecular layers, which might be oxidatively degraded.

For a sensor application the affinity materials should exhibit both, affinity and selectivity. The latter is necessary for discrimination of TATP over potentially interfering compounds. Thus, a selection of analytes was screened, including acetone and hydrogen peroxide, as starting materials for the preparation of TATP. If no strong acid is present TATP will not be in equilibrium with the starting materials. Bis-*tert*-butyl peroxide served as a lipophilic and structurally related peroxide. Water represents an omnipresent compound in real-life scenarios. From the individual affinities the selectivity (S) in respect to TATP was calculated:^[6,20]

$$S = \frac{Affinity_{analyte}}{Affinity_{TATP}}$$

Only the dendrimers with a considerably higher affinity towards TATP than **1** are depicted with their selectivity in Figure 2. The relative intensity for TATP with the quantity of 1.0 is not displayed in Figure 2. Almost all selected dendrimers, except **2b** and **12**, show the same low affinity for acetone. The lowest affinities for bis-*tert*-butyl peroxide are seen for the dendrimers **5** and **3b**. In addition to this, **5** exhibits the lowest



Figure 2. Selectivity of the best affinity materials normalized on TATP. For TATP the relative intensity is S = 1.0 and is omitted for clarity.

cross-affinities for water as well as hydrogen peroxide. This remarkable selectivity of **5** is not only attributed to the absence of heteroatoms because the same applies to **12** which show the highest affinity towards the four interference analytes. The dendrimers **5** and **3b** combine the highest affinity for TATP with the lowest cross-sensitivities, at which **5** has the smaller affinity especially for water, which is the most common interference for artificial noses. Consequently, compound **5** is the most promising candidate for application in a TATP sensor.

In conclusion, the preparation of novel polyphenylene-type dendrimers led to affinity materials superior to the gold standard for TATP tracing by QCM. With incorporation of pyrenyl and cyanophenyl units not only the affinity to TATP was dramatically enhanced but also the selectivity over interfering compounds was ameliorated allowing an exquisite discrimination for TATP. Furthermore, the downsized dendrimers **4a** and **5** are capable of outperforming larger structures in terms of overall TATP affinity, which was so far believed to be the specialty of widely branched nanoparticles.^[6] Thus, the short synthesis of small highly functionalized dendrimers is more cost and time efficient compared to the preparation of G_4 dendrimers. The nonpolar and pyrenyl containing dendrimer **5** displays best overall characteristics for the detection of TATP, thus representing a superior material for device construction. In an open device the limit of detection by **5** is 3σ = 31 ppb TATP. For the supramolecular recognition of TATP the conformational restrictions of the voids in the dendrimers seems to be crucial by providing more defined incorporation sites.

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